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U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NO
POGGE VON STRANDMANN (PCT)

U S APPLICATION NO (if known, see 37 CFR 1 5)
10/019708

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/01822	FEBRUARY 22, 2000	FEBRUARY 25, 1999

TITLE
PREPARATION FOR THE TREATMENT OF PIGMENTATION DISORDERS

APPLICANT(S) FOR DO/EO/US
ELKE POGGE VON STRANDMANN

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. X This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ___ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. X This is an express request to begin national examination procedures (35 U.S.C. 371 (f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(l).
4. X A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. X A copy of the International Application as filed (35 U.S.C. 371(c)(2)
   a. X is transmitted herewith (required only if not transmitted by the International Bureau)
   b. ___ has been transmitted by the International Bureau.
   c. ___ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. X A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ___ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
   a. ___ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ___ have been transmitted by the International Bureau.
   c. ___ have not been made; however, the time limit for making such amendments has **NOT** expired.
   d. ___ have not been made and will not be made.
8. ___ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. X An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ___ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. X An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ___ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. X A **FIRST** preliminary amendment.
    ___ A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. ___ A substitute specification.
15. ___ A change of power of attorney and/or address letter.
16. X Other items or information:

    PCT/ISA/210 - Int'l. Search Report (English)
    3 Sheets of Formal Drawings
    PETITION TO REVIVE

Applicant Claims Priority under 35 U.S.C. §119 of German Application Nos. 199 08 242.1 and 199 34 458.2 filed February 25, 1999 and July 27, 1999, respectively.
Applicant Claims Priority under 35 U.S.C. §120 of: PCT/EP00/01822 filed February 22, 2000.

APPLICATION NO. (if known, see 37 CFR 1 5) 10/019708	INTERNATIONAL APPLICATION NO PCT/EP00/01822	ATTORNEY'S DOCKET NO POGGE VON STRANDMANN (PCT)
_X_ The following fees are submitted **Basic National Fee (37 CFR 1.492(a)(1)-(5)):**	CALCULATIONS	PTO USE ONLY
Search Report has been prepared by the EPO or JPO..... **$890.00**		
International preliminary examination fee paid to USPTO (37 CFR 1 482) **$710.00**		
Neither international preliminary examination fee paid (37 CFR 1 82) nor international search fee (37 CFR 1 445(a)(2)) paid to USPTO **$1,040.00**		
International preliminary examination fee paid to USPTO (37 CFR 1 482) and all claims satisfied provisions of PCT Article 33(2)-(4) **$100.00** **ENTER APPROPRIATE BASIC FEE AMOUNT =**	$ 890 00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ___ 20 ___ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		

Claims	Number Filed	Number Extra	Rate		
Total Claims	10 - 20 =	- 0 -	X **$18.00**	$	
Independent Claims	1 - 3 =	- 0 -	X **$84.00**	$	
Multiple dependent claim(s) (if applicable)			+ **$280.00**	$	
TOTAL OF ABOVE CALCULATIONS =				$ 890 00	
Reduction by 1/2 for Small Entity status				$ 445 00	
SUBTOTAL =				$ 445 00	
Processing fee of **$130.00** for furnishing the English translation later than ___ 20 ___ 30 months from the earliest claimed priority date (37 CFR 1 492(f)) +				$	
TOTAL NATIONAL FEE =				$ 445 00	
Fee for recording the enclosed assignment (37 CFR 1 21(h)) The assignment must be accompanied by an appropriate cover sheet (37 CFR 3 28, 3.31) **$40.00** per property +				$ 40 00	
TOTAL FEES ENCLOSED =				$ 485.00	
				Amount to be refunded	$
				charged	$

_X_ Applicant claims Small Entity status.

a. _X_ A check in the amount of $ 485.00 to cover the above fees is enclosed.

b. ___ Please charge my Deposit Account No. 03-2468 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. _X_ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 03-2468. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
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Edward R. Freedman
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Express Mail No. **EL 871 451 067 US**
Date of Deposit December 27, 2001
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Lisa L. Vulpis

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: ELKE POGGE VON STRANDMANN (PCT)

PCT No.: PCT/EP00/01822 FILED: FEBRUARY 22, 2000

TITLE: PREPARATION FOR THE TREATMENT OF PIGMENTATION DISORDERS

PRELIMINARY AMENDMENT

BOX PCT
U.S. Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

Preliminary to Examination, please amend the above-identified application as follows:

IN THE SPECIFICATION

Page 1, after the title, please insert as follows:

--CROSS REFERENCE TO RELATED APPLICATIONS

Applicant claims priority under 35 U.S.C. §119 of German Application Nos. 199 08 242.1 and 199 34 458.2 filed February 25, 1999 and July 27, 1999, respectively. Applicant also claims priority under 35 U.S.C. §120 of PCT/EP00/01822 filed February 22, 2000. The international application under PCT article 21(2) was not published in English.--

IN THE CLAIMS

Please amend the claims as follows:

4. (Amended) The preparation according to claim 1, characterized in that the excipient contains a transfer medium transporting the active ingredient.

6. (Amended) The preparation according to claim 1, characterized in that it is present in the form of a formula for topical application.

7. (Amended) The preparation according to claim 1, characterized in that it is present in the form of an injection formula.

8. (Amended) The preparation according to claim 1, characterized in that it is intended for the pigmentation or de-pigmentation of skin or hair.

10. (Amended) The use of the protein DCoH, the DNA and/or RNA for the coding of said protein, or DCoH antibodies or DCoH antiserum, as active ingredient for producing a preparation according to claim 1 for the treatment of pigmentation disorders of the human or animal body.

A marked-up version of the claims is shown as Exhibit A.

Please add the Abstract, attached hereto on a separate sheet.

REMARKS

By this Preliminary Amendment, a cross-reference to related applications has been inserted in page 1. The claims have been amended so that the multiple dependency of certain of the dependent claims have been removed to avoid the surcharge associated therewith, and an Abstract is being provided. No new matter has been introduced. Entry of this amendment is respectfully requested.

Respectfully submitted,
ELKE POGGE VON STRANDMANN

By: _____
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Enclosure: Exhibit A and an Abstract
EXPRESS MAIL NO. **EL 871 451 067 US**
Date of Deposit: December 27, 2001
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10, on the date indicated above, and is addressed to BOX PCT, U.S. Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202.

Lisa L. Vulpis

ABSTRACT OF THE DISCLOSURE

The invention relates to a preparation for the treatment of pigmentation disorders. The preparation contains a physiologically active quantity of the DCoH protein, the DNA and/or RNA coding for the protein or DCoH antibodies or antiserum as active ingredient in a pharmaceutically suitable excipient. The invention also relates to the use of DCoH, the DNA and/or RNA coding for same or DCoH antibodies or antiserum as active ingredient in the production of such a preparation.

EXHIBIT A

VERSION WITH MARKINGS TO SHOW CHANGES MADE TO CLAIMS 4, 6-8, and 10

4. The preparation according to [claims 1, 2 or 3] claim 1, characterized in that the excipient contains a transfer medium transporting the active ingredient.

6. The preparation according to [any one of the preceding claims] claim 1, characterized in that it is present in the form of a formula for topical application.

7. The preparation according to [any one of claims 1 to 4] claim 1, characterized in that it is present in the form of an injection formula.

8. The preparation according to [any one of the preceding claims] claim 1, characterized in that it is intended for the pigmentation or de-pigmentation of skin or hair.

10. The use of the protein DCoH, the DNA and/or RNA for the coding of said protein, or DCoH antibodies or DCoH antiserum, as active ingredient for producing a preparation according to [any one of claims 1 to 8] claim 1 for the treatment of pigmentation disorders of the human or animal body.

3/prts

PREPARATION FOR THE TREATMENT OF PIGMENTATION DISORDERS

The invention relates to a preparation for the treatment of pigmentation disorders of the human and animal body with the use of the protein DCoH and the DNA and/or RNA coding for said protein as the active ingredient.

The enzyme DCoH of the dimerization factor of the HNF-1 homeodomanial proteins (HNF-1∝ and HNF-1ß). DCoH is participating by means of said mechanisms in the control of the gene expression (see D.B. MENDEL ET AL in Science 254 (1991; page 1762). The protein is known at the same time as the ptrin-4∝-carbinolamine-dehydratase PCD and participates in the tetrahydrobiopterin regeneration (see B.A. CITRON ET AL, Proc. Natl. Acad. Sci. USA 89; 1992; page 11891). PCD engages in the process of the biosynthesis of L-tyrosine from L-phenylalanine. In the latter cycle, PCD is tied in together with phenyl-alanine hydroxylase and participates in the regeneration of (6R)5,6,7,8-tetrahydrobiopterin. Independently thereof, however, DCoH/PCD is found also in the vertebral El. and in the pigmented epithelium of the eye, and in the skin and the brain - see E. POGGE V. STRANDMANN and G.U. RYFFEL, Development 121 (1995); page 1217; E. POGGE V. STRANDMANN ET AL in Int. J. Dev. Biol. 42 (1998) page 53).

After the first data on the purification and cloning of DCoH were supplied by D.B. MENDEL ET AL in Science 254 (1991), page 1762, both the peptide sequence and the nucleic acid sequence of human, mouse and rat-DCoH coding for said protein have been described for the first time in US-A-5,403,712 and 5,620,887. Reference is made to said patents with respect to all relevant structural data. DCoH/PCD has been found to be a more or less universal principle in the development of vertebrae, in particular also for their early development. It possesses both catalytic as well as regulating properties and is present in a greater number of types of cells. It is closely associated in some of said cell types with the nuclear transcription factors HNF-1α and HNF-1ß, and in other cell types it is tied into the phenylalanine-hydroxylase enzyme complex. The presence of DCoH/PCD in cell types in the absence of HNF-1 or phenylalanine-hydroxylase suggests that the protein also cooperates with cellular partners that are different from those cell types.

Vitiligo, for example, is a known pigmentation disorder. Vitiligo is characterized by white, pigment-free, mostly gradually growing patches with a hyperpigmented edge and is attributed to an inhibition of the melanin synthesis. The phenomenon may occur in conjunction with other diseases such as diabetes mellitus. No causal treatment has been

possible until now. Vitiligo seems to be associated with an insufficiency of DCoH.

Other pigmentation disorders are, for example forms of canities, i.e. grayness of the hair, both in the physiological form occurring prematurely and at higher age levels. In this instance, too, no causal therapies are known.

A disease that is linked with phenomena of de-pigmentation is alopecia areata, which is a local, suddenly beginning and causally unclear loss of hair, in particular also of the hair of the head. In connection with this type of loss of hair, the hair follicles are preserved, but remissions occur spontaneously in the course of which the affected hair is (first) growing again white. The disease is therefore connected with a pigmentation disorder.

Furthermore, the Usher syndrome and the Waardenburg syndrome are connected with pigmentation disorders. Moreover, numerous disorders are known that are connected with (local) hyperpigmentation.

The effects of the phenomena and diseases mentioned above have been described in great detail; however, it has not been possible to clarify their causes. The assumption

that the peptide DCoH/PCD might play a role in this connection has been expressed with respect to vitiligo; however, this has not been proven. Many factors do in fact suggest that the reduction of the enzymatic activity of DCoH observed in connection with mild forms of hyperphenylalaninemia and vitiligo may be a consequence but not the cause of said disorders. It has been proven that an excess supply of the cofactor tetrahydrobioterine required for the formation of L-tyrosine from L-phenylalanine is present in the affected cells.

Overall, there is a need for preparations that are suited for the treatment of pigmentation disorders of the human and animal body and of the phenomena connected with such disorders.

It has now been surprisingly found that DCoH/PCD is suitable for creating de novo pigmented cells. In this process, DCoH is not a link in the melanin synthesis whose absence leads to de-pigmentation, but an "artificial hyper-expression" takes place that triggers the pigmentation. Furthermore, it has been found that DCoH antiserum is suited for weakening pigmentation or for preventing it (its occurrence).

Therefore, the object of the invention is a preparation for the treatment of pigmentation disorders in which a physiologically active amount of the protein DCoH, of the DNA and/or RNA coding for said protein, or of DCoH-antibodies is contained as the active ingredient in a pharmaceutically acceptable excipient.

The preparation as defined by the invention contains the protein DCoH triggering the pigmentation, or as an alternative or supplement the DNA and/or RNA coding for said protein, or as an alternative DCoH-antibodies or antiserum as the active ingredients.

The effect of DCoH/PCD has been demonstrated experimentally after mRNA was injected into oocytene. Since the RNA in the cell is the product of the transcription of the corresponding DNA, and is itself transformed into the protein, the efficiency of all three active ingredients, i.e. of the protein, the DNA and the RNA, is secured, whereby certain spectra may occur with respect to the intensity and duration of the effect. The protein sequence and the nucleic acid sequence of DCoH and of the DNA coding for said protein are described in US-A-5,403,712 and 5,620,887. The preparation of antiserum has been described in Development 121, page 1217 (1995). In detail, both poly-

and monoclonal antibodies can be considered for the purpose as defined by the invention.

The preparation as defined by the invention for the treatment of pigmentation disorders contains the active ingredient in a usually employed, pharmaceutically acceptable and compatible excipient. Such excipients are known both for topical and parenteral administration. Possible are, furthermore, gene-therapeutic forms of administration in connection with which the gene decoding for the DCoH is introduced into the target cell. The concentrations of the active ingredient are the same as commonly applied in the field of protein/DNA/RNA therapy and are oriented on the concentrations normally found in the target cells, i.e. such concentrations are at the normal level or higher.

In topical administrations, the preparation can be applied to the skin, whereby the active ingredient is contained in a transdermally effective excipient. Such excipients, which are conceived in the present case in the form of penetration aids or penetration accelerators and present in most cases in the form of liposomes, are known. Furthermore, the preparation may be applied by means of a transdermal system, which is useful particularly in the treatment of local disorders.

In topical applications that are directed at certain regions or cells, for example in connection with hyper-pigmented or de-pigmented regions of the skin or areas of hair growth, especially the application of liposomes developed for that purpose is recommended, such as the liposomes described by R.M. HOFFMAN in the Journal of Drug Targeting, vol. 6 (1997), 67. HOFFMANN describes the hair follicle-selective introduction of macromolecules up to the active gene with a target system based on topically applied liposomes based on phosphatyl choline. The system is applicable to melalins, proteins, genes and the like introduced into liposomes or bonded to the latter.

Cationic lipids for the intracellular dispensing of biologically active molecules are known, furthermore, from WO-A 91/16024, whereby such cationic lipids can be employed for the topical, enteral and also parenteral administration of active ingredients.

It may be useful in many cases to make the active ingredient available systemically in a manner as it is known, for example from the interferon-therapy of multiple sclerosis or also in the treatment of diabetes. Said therapies are based on the uniform distribution of the active ingredient in the body and the effect triggered by such uniform distribution. The active ingredient can be used

in this connection as such or also in a modified form, i.e. in forms that release the actual active ingredient only in the target site. Suspensions for parenteral administration usefully contain the active ingredient also bonded to or included in liposomes acting as the transfer medium, and suspended in a physiologically acceptable carrier liquid.

Another systemic form of administration, for example, is in the form of a nasal spray that transports the active ingredient onto the mucous membranes and delivers it to the body via such mucous membranes.

Another administration possibility is the implantation of pro- or eucaryotic organisms or of excipients containing the active ingredient. Such excipients secrete the active ingredient at a continuous or regulated rate.

Finally, reference is made to the possibilities offered by the gene therapy, i.e. the embedding of the gene for DCoH/PCD in a target cell by means of DNA- or RNA-viruses, which integrate into the genome and in this way introduce the gene in a stable manner. The gene is then subject to the normal transcription and translation into the cell and thus represents a useful alternative to transient transfection with the protein, or the DNA or RNA coding for said protein. The viruses may embed themselves in this connection locally

(see also the p53-deficiency of melanomas), or may spread through the body in an undirected manner. Adenoviruses or other "cold viruses" that are modified for said purpose are described in the prior art and may be considered as suitable vehicles. Antisense techniques may be employed for excluding hyper-pigmentation.

It is understood that the protein or the DNA and/or RNA coding for said protein may be stabilized for storage purposes and for the purpose of avoiding any premature deterioration of the effect. Stabilization can be accomplished by adding the usual additives such as, for example buffer substances, salts of other proteins, as well as also salts of DNA and RNA. For example albumin, herring sperms, DNA and tRNA are known for said purpose from the field of molecular biochemistry, and also by adding detergents (thesiteR, tritonR), alkali and alkaline earth ions and the like. Storing the preparation and/or active ingredient in the dried or freeze-dried form, or after flash-freezing in liquid nitrogen may be useful as well.

The preparation as defined by the invention may, of course, contain the active ingredient in the modified form as well, i.e. in the form of protein in which individual amino acids are exchanged or missing. Likewise, nucleotides or nucleotide sequences may be missing, supplemented or

exchanged in the DNA and/or the RNA. The precondition is that the active ingredient so modified will continue to still deliver the effect it is expected to supply in the treatment of de-pigmentation phenomena. Reasons for such modifications may be the stabilization of the active ingredient, production technology-related or formulation-technical grounds, or also an enhancement of the effect or spectrum of effects. Considered may be mutation and fusion according to gene-technological or chemical methods, as well as fusion with N- and C-terminal proteins or peptides. For reasons of superior purification by means of affinity chromatography, it is possible also to carry out, for example histidine tags or Gst fusions, or to insert sequences in order to facilitate the direction into defined target cells. NLS-sequences are suitable for directing the active ingredient into the core of the cell. By means of phosphorylation or glycolization on suitable radicals, and with the help of modifications on the phosphate group of the DNA or RNA it is possible also to effect modifications that prevent the degradation by the body's own nucleases. Phosphorus-thioate groups are known for said purpose.

For stabilizing the protein it may be useful to introduce changes, for example already at the level of the DNA/RNA, for example in order to eliminate sites of restriction, chemical instability, or points of attack of

nucleases, or to intensity or specify the effect, for example also in order to discriminate between the various activities of the multifunctional protein, as well as for the purpose of deactivating an interfering function. Vice versa, it may be useful to reduce the stability and to thus reduce the half-time value of the active ingredient by introducing modifications that permit protolytic degradation, for example by incorporating recognition sequences for detecting proteases.

The protein can be isolated in the usual manner following cloning of the gene in suitable vectors recombined from bacteria or eucaryonts. The DNA and the RNA can be obtained from bacteria or eucaryonts according to standard methods.

The preparation as defined by the invention for the treatment of pigmentation disorders contains the active ingredient in a pharmaceutically acceptable excipient that may be comprised of several of the usual components, on the one hand. The excipient in turn usefully contains a transfer medium suitable for the active ingredient, in particular a liposome or a virus. The preparation is primarily intended for topical or parenteral administration.

In addition to a preparation for treating pigmentation disorders, the invention also relates to the use of DCoH, the DNA and/or RNA coding for said protein, or DCoH antibodies or DCoH antiserum as the active ingredient for the preparation of a medication for treating pigmentation disorders of the human and the animal body. In particular, pigmentation disorders are understood to constitute de-pigmentation phenomena of the skin, hair and the retina, including in particular vitiligo, alopecia areata, as well as the premature or age-conditioned graying of the growth of hair, and also forms of local hyperpigmentation such as, for example melanoderma, nevus and the like. The invention relates to both congenital and acquired pigmentation disorders.

Another field of application of the DCoH as defined by the invention, the DNS and/or RNA coding for said protein, or DCoH antibodies or DCoH antiserum containing the preparation is the treatment of melanocytic tumors. Melanocytic tumors and in particular also the malignant melanoma represent de-differentiated melanocytes of clonal origin.

The preparation as defined by the invention is acting on melanocytic tumors in two directions. On the one hand, its effect is based on the re-differentiation of de-

differentiated melanocytes. Tests on xenopus oocytes have shown that DCoH initiates the differentiation of melanocytes. The application of the preparation as defined by the invention thus acts in the direction of re-differentiation and normalization of degenerated cells.

On the other hand, it is possible to influence the division of the melanocytes via suitable mutants of the DCoH-DNA, DCoH-RNA or the protein itself. Via blocking of the effect of the DCoH it is possible to influence the rate of division of the melanocytes up to standstill of the division, and even up to killing the cells.

The invention is explained in greater detail in the following, whereby reference is supplementarily made to E. POGGE VON STRANDMANN and G.U. RYFFEL, Development 121 (1995), pages 1217 to 1226.

Example 1

Frogs of the Xenopus species were maintained under standard conditions. For in vitro insemination, 600 U gonadotrophin (human) was subcutaneously injected into the dorsal lymph sac of sexually mature females; the eggs were placed in Petri dishes and then fertilized with intact sperms. After 5 minutes, top coating was carried out with 88

mM NaCl, 1 mM KCl, 0.7 mM CaCl , 1 mM MgSO , 5 mM Hepes ph 7.8, and 2.5 mM NaHCO .

For the micro-injection, the gel coat was removed and then treated for 1.5 minutes with 2% cysteine at ph 8.0, and subsequently washed three times in top coating buffer. Following the injection, cultivation was carried in overcoating buffer at room temperature.

mRNA obtained by in vitro transcription from suitable recombined vectors was used for the injection. 500 pg/RNA in 25 nl buffer solution was injected per egg. The small glass tubes used for said purpose were drawn from capillaries prior to their use and had a diameter of not more than 30 µm at the tip.

The embryos developed from the eggs exhibited a distinct pigmentation that started earlier than in the control stage. Furthermore, pigmentation occurred in sites where the embryo is normally not pigmented.

FIG. 1 shows embryos that over-express DCoH in the left row of the images (A/C). The control is located on the right row of images (B/D). The dark pigmentation patches are clearly visible in the left row of images. The abbreviations

designate the following: a = anima; eye = eye; cg = cement glant.

DCoH/PCD thus induces ectopic pigment cells. The result shows that DCoH/PCD alone, i.e. without the melanin synthesis chain, is capable of triggering the steps required for the pigment synthesis.

Example 2

In the present example, the RNA for the DCoH in xenopus embryos in the 2 cell stage is injected only into one of the two cells, together with the RNA's for the GFP = green fluorescent protein. The co-injection of the RNA for the GFP served the purpose of visualizing that the injected RNA's are also translated into active protein only in the injected cells.

FIG. 2 shows that in the larvae developing from the second cell stage, the pigmentation is limited to one half of the body of the larvae, namely where the fluorescence is visible as well (right-hand row of images). DCoH/PCD is thus suited to trigger a premature pigmentation and pigmentation beyond the normal measure in the cells into which it was admitted. The larvae developed in a normal manner disregarding the hyperpigmentation and the fluorescence.

Example 3

Antiserum against DCoH obtained according to standard methods in rabbits was injected analogous to example 2 into cells of frogs of the xenopus species. FIG. 3 shows that the formation of pigmentation is completely suppressed in embryos three days old (∝-DCoH, top image), whereas the normal pigmentation appears in the control (bottom image).

Patent Claims:

1. A preparation for the treatment of pigmentation disorders of the human and animal body, characterized in that it contains a physiologically active amount of the protein DCoH, the DNA and/or RNA coding for said protein, or DCoH antibodies or DCoH antiserum in a pharmaceutically acceptable excipient.

2. The preparation according to claim 1, characterized in that it contains the protein DCoH.

3. The preparation according to claim 1, characterized in that it contains DCoH antibodies.

4. The preparation according to claims 1, 2 or 3, characterized in that the excipient contains a transfer medium transporting the active ingredient.

5. The preparation according to claim 4, characterized in that the transfer medium is a liposome preparation or a virus.

6. The preparation according to any one of the preceding claims, characterized in that it is present in the form of a formula for topical application.

7. The preparation according to any one of claims 1 to 4, characterized in that it is present in the form of an injection formula.

8. The preparation according to any one of the preceding claims, characterized in that it is intended for the pigmentation or de-pigmentation of skin or hair.

9. The preparation according to claim 8 intended for the treatment of vitiligo, alopecia areata and/or canities or melanoderma.

10. The use of the protein DCoH, the DNA and/or RNA for the coding of said protein, or DCoH antibodies or DCoH antiserum, as active ingredient for producing a preparation according to any one of claims 1 to 8 for the treatment of pigmentation disorders of the human or animal body.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
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Veröffentlicht:
— *Mit internationalem Recherchenbericht.*

(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 14. Dezember 2000

Zur Erklärung der Zweibuchstaben-Codes, und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(54) Title: PREPARATION FOR THE TREATMENT OF PIGMENTATION DISORDERS

(54) Bezeichnung: MITTEL ZUR BEHANDLUNG VON PIGMENTIERUNGSSTÖRUNGEN

(57) Abstract: The invention relates to a preparation for the treatment of pigmentation disorders. Said preparation contains a physiologically active quantity of the DCoH protein, the DNA and/or RNA coding for said protein or DCoH antibodies or antiserum as active ingredient in a pharmaceutically suitable excipient. The invention also relates to the use of DCoH, the DNA and/or RNA coding for same or DCoH antibodies or antiserum as active ingredient in the production of such a preparation.

(57) Zusammenfassung: Die Erfindung betrifft ein Mittel zur Behandlung von Pigmentierungsstörungen, das eine physiologisch wirksame Menge des Proteins DCoH der dafür codierenden DNA und/oder RNA oder DcoH-Antikörper oder -Antiserum als Wirkstoff in einem pharmazeutisch annehmbaren Trägermaterial enthält, sowie die Verwendung von DCoH der dafür codierenden DNA und/oder RNA oder von DcoH-Antikörpern oder -Antiserum als Wirkstoff zur Herstellung solch eines Mittels.

WO 00/50070 A3

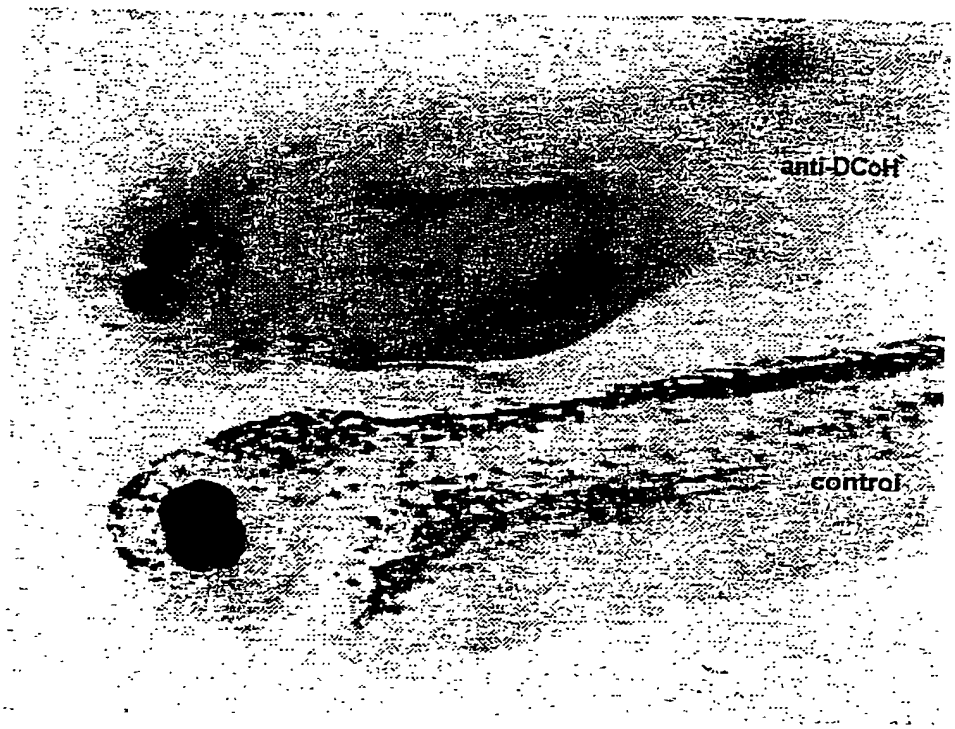

FIGURE 3

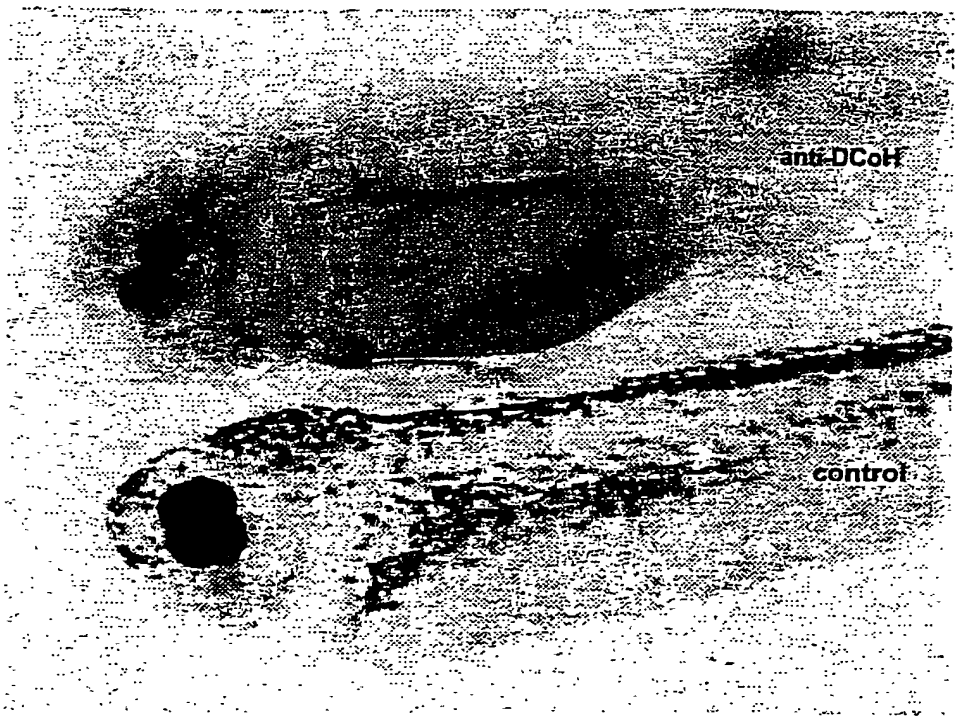

FIGURE 3

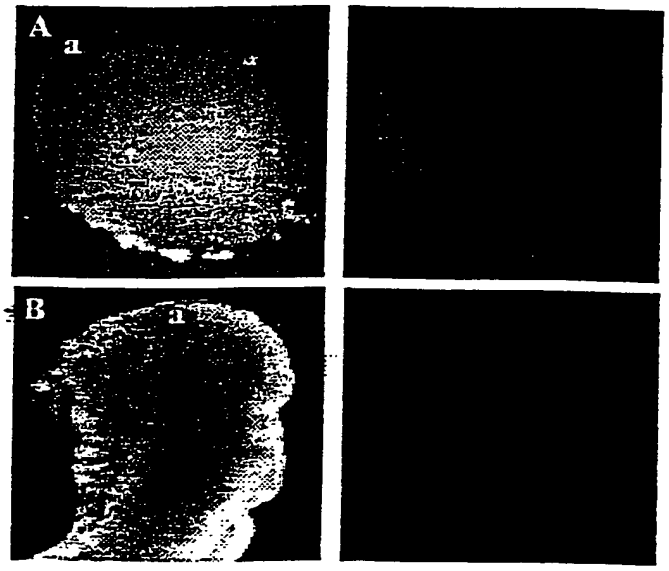

FIGURE 2

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

ATTORNEY'S DOCKET NUMBER
POGGE VON STRANDMANN- PCT

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

PREPARATION FOR THE TREATMENT OF PIGMENTATION DISORDERS

the specification of which (check only one item below):

[ ] is attached hereto.

[ ] was filed as United States application

Serial No. _____

on _____,

and was amended

on _____ (if applicable).

[X] was filed as PCT international application

Number PCT/EP00/01822

on 22 FEBRUARY 2000,

and was amended under PCT Article 19

on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 U.S.C. 119
GERMANY	199 08 242.1	25 FEBRUARY 1999	[X] YES [ ] NO
GERMANY	199 34 458.2	27 JULY 1999	[X] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY
(Includes Reference to PCT International Applications)

ATTORNEY'S DOCKET NUMBER
POGGE VON STRANDMANN- PCT

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

(Application Number) (Filing Date)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclose in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code. §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS (Check One)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

PCT APPLICATIONS DESIGNATING THE U.S					
PCT APPLICATION NO	PCT FILING DATE	U.S. SERIAL NUMBERS ASSIGNED (if any)			

POWER OF ATTORNEY. As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (List name and registration numbers):
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0	RESIDENCE & CITIZENSHIP	CITY: BOCHUM DEX	STATE OR FOREIGN COUNTRY: GERMANY	COUNTRY OF CITIZENSHIP: GERMANY
1	POST OFFICE ADDRESS	POST OFFICE ADDRESS: MORITZSTRASSE 14	CITY: D-44807 BOCHUM	STATE & ZIP CODE/COUNTRY: GERMANY

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201
x Elke Pogge v. Strandmann

DATE
x 19. Oktober 2001

R:\Vita\Ingrid\Pogge Von Strandmann-PCT decl.wpd